

Variability in mortality following caesarean delivery, appendectomy, and groin hernia repair in low-income and middle-income countries: a systematic review and analysis of published data

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Summary

Background Surgical interventions occur at lower rates in resource-poor settings, and complication and death rates following surgery are probably substantial but have not been well quantified. A deeper understanding of outcomes is a crucial step to ensure that high quality accompanies increased global access to surgical care. We aimed to assess surgical mortality following three common surgical procedures—caesarean delivery, appendectomy, and groin (inguinal and femoral) hernia repair—to quantify the potential risks of expanding access without simultaneously addressing issues of quality and safety.

Methods We collected demographic, health, and economic data for 113 countries classified as low income or lower-middle income by the World Bank in 2005. We did a systematic review of Ovid, MEDLINE, PubMed, and Scopus from Jan 1, 2000, to Jan 15, 2015, to identify studies in these countries reporting all-cause mortality following the three commonly undertaken operations. Reports from governmental and other agencies were also identified and included. We modelled surgical mortality rates for countries without reported data using a two-step multiple imputation method. We first used a fully conditional specification (FCS) multiple imputation method to establish complete datasets for all missing variables that we considered potentially predictive of surgical mortality. We then used regression-based predictive mean matching imputation methods, specified within the multiple imputation FCS method, for selected predictors for each operation using the completed dataset to predict mortality rates along with confidence intervals for countries without reported mortality data. To account for variability in data availability, we aggregated results by subregion and estimated surgical mortality rates.

Findings From an initial 1302 articles and reports identified, 247 full-text articles met our inclusion criteria, and 124 provided data for surgical mortality for at least one of the three selected operations. We identified 42 countries with mortality data for at least one of the three procedures. Median reported mortality was 7·9 per 1000 operations for caesarean delivery (IQR 2·8–19·9), 2·2 per 1000 operations for appendectomy (0·0–17·2), and 4·9 per 1000 operations for groin hernia (0·0–11·7). Perioperative mortality estimates by subregion ranged from 2·8 (South Asia) to 50·2 (East Asia) per 1000 caesarean deliveries, 2·4 (South Asia) to 54·0 (Central sub-Saharan Africa) per 1000 appendectomies, and 0·3 (Andean Latin America) to 25·5 (Southern sub-Saharan Africa) per 1000 hernia repairs.

Interpretation All-cause postoperative mortality rates are exceedingly variable within resource-constrained environments. Efforts to expand surgical access and provision of services must include a strong commitment to improve the safety and quality of care.

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Introduction

Surgery is an essential component of a functioning, comprehensive health system, but also a high-risk intervention. Recent work has estimated that 312·9 million operations occur annually, with most taking place in upper-middle-income and high-income countries.¹ Countries with more than 35% of the world's population account for only 6·3% of the total operations, probably indicating a vast unmet need for surgical care in these settings. Additionally, the safety of such care is known to be extremely variable with a presumably high proportion of preventable deaths.²

Many health interventions in low-income and middle-income countries have focused on infectious diseases and maternal and child health. Substantial improvements have been made through programmes developed within growing health systems (eg, developing cadres of skilled birth attendants) or in parallel to poorly functioning ones (eg, vaccination campaigns and directly observed therapy for tuberculosis and HIV).^{3–8} However, populations traditionally affected by infectious diseases and malnutrition are now also faced with the health problems of industrialisation and ageing.⁹ Yet the

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Research in context

Evidence before this study

Wide variability in postoperative mortality has been described in countries with substantial health and financial resources; however, little research has been done on the variability in postoperative mortality in low-income and middle-income countries. We searched OVID, PubMed, MEDLINE, and Scopus to identify articles published in 2000 or later that provided mortality information following caesarean delivery, appendectomy, and groin hernia repair in countries classified as either low income or lower-middle income (LMICs) by the World Bank in 2005, and included articles published in English, Spanish, or French that reported mortality following one of these interventions regardless of preoperative status, urgency of intervention, indication for procedure, or cause of death. We originally undertook this study as a result of our observations of excessively high death rates reported following surgery in LMICs, and recognised the need for a deeper understanding

of the range of mortality rates following surgery. Almost nothing has been written about this on a global scale.

Added value of this study

This study provides evidence of tremendous variability in mortality following three common operations, and signals a potential area for focused efforts to improve safety and quality of care. Compared with the Netherlands who have some of the lowest reported mortality in the world, we noted a relative risk of death following surgery as high as 22.2 for caesarean delivery, 2.4 for appendectomy, and 1.8 for groin hernia repair.

Implications of all the available evidence

Although several factors prevent direct comparisons of outcomes between rich and poor countries, the fact that the range in death rates amongst LMICs is so variable indicates that improvements are possible even with the resource constraints faced by many health systems.

sophisticated and coordinated care required to confront these health issues will require considerable health system development in the next few decades.^{10,11} Surgical care is particularly complex, and its performance requires organisation and management of several clinical and administrative departments within a facility. Because of this, access to surgical care is frequently absent, and typically low on the list of priorities for public health intervention. Additionally, services that are provided are of variable quality and might in fact contribute to health burden.¹²

Several barriers to improving surgical capacity exist. Surgery requires infrastructure and consumable and durable resources with an effective supply chain, advanced skills, and a robust training programme for providers, along with management practices that allow the coordination of complex care. Many health systems in resource-poor settings do not have capacity in at least one of these domains.^{13–15} As health systems improve surgical capacity, concerns regarding quality and safety will be ongoing. Previous studies in high-income nations have already shown significant differences in outcomes of surgical care, both between countries and within countries.^{16,17} Yet little focus has been paid to the outcomes of surgical care in low-income and middle-income countries. We aimed to assess surgical mortality following three common surgical procedures—caesarean delivery, appendectomy, and groin (inguinal and femoral) hernia repair—to quantify the potential risks of expanding access without simultaneously addressing issues of quality and safety.

Methods

Population and health data

We collected population, health, demographic, and economic information from the WHO for all 113 countries

classified as low or lower-middle income (LMICs) by the World Bank in 2005. We obtained total population size, life expectancy, maternal mortality ratios, under-5 mortality, physician and nursing density, number of hospital beds, gross domestic product, per capita expenditure on health, literacy rates, urban versus rural population size, and proportion of the population younger than 15 years. We also collected geographic information, including country size and road infrastructure, from the Central Intelligence Agency *World Factbook*.¹⁸ We further collected information about corruption from Transparency International, and financial inequality using the Gini coefficient, a measure of the inequality of income distribution, from the World Bank. We also categorised countries by the six WHO regions and by the 21 Global Burden of Disease (GBD) regions.

We expected surgical deaths would be increased in LMICs for one of five reasons: (1) prehospital delays that included geographic location, distance, transportation challenges, financing, cultural factors, and other care-seeking behaviours; (2) delays during hospital admission that included absence of financing, failure of appropriate triage, and cultural factors, stereotyping, and barriers inhibiting care for vulnerable populations; (3) infrastructure and resource limitations including absence of skilled providers, of durable and consumable goods, material, or medications, and of sterility and equipment; (4) absence of management and organisational structure including inability to organise services appropriately or provide guidance and direction for goal-oriented and outcomes-driven care and services; and (5) other unknown elements and components of care that affect health-seeking behaviour and service delivery.^{15,18–22} We chose country-level variables a priori to represent these issues as follows:

For the World Bank Open Data country corruption data see <http://data.worldbank.org/>

For the Transparency International country corruption data see <http://www.transparency.org/country>

For the Global Burden of Disease data see <http://www.globalburden.org>

For the WHO Global Health Observatory data repository see <http://apps.who.int/gho/data/node.home>

(1) ratio of paved roads to country surface area, access to water; (2) Gini index, health expenditure; (3) physician density, nurse and midwife density, births by caesarean delivery, surgical rates, pulse oximetry availability or density, hospital beds; (4) corruption index; and (5) life expectancy, pregnancy and childbirth mortality, and under-5 mortality.

Surgical mortality data

We did a systematic review (PROSPERO registration number: CRD42015015837) using PRISMA guidelines.²³ We comprehensively searched Ovid, PubMed, MEDLINE, and Scopus in English, French, and Spanish, with additional reference capture from Google Scholar to identify articles from Jan 1, 2000, to Jan 15, 2015, reporting surgical mortality from LMICs (as defined by the World Bank in 2005) for caesarean delivery, appendectomy, or groin hernia repair. We chose these procedures because they are commonly undertaken, have a clear diagnostic indication, and are often done in a select group of patients. We selected the year 2000 as a cutoff because of the temporal trend of improvements in perioperative mortality; we attempted to reflect the most recent data for perioperative mortality by limiting the analysis to the last 15 years. Search terms included “caesarean delivery” along with related terms and alternative spelling; “appendectomy” along with related terms and alternative spellings, “hernia repair” or “herniorrhaphy” along with related terms and spellings; “maternal mortality” or “death” or “mortality”; and “low and lower middle income countries” or “developing countries” along with related terms as well as individual country names that met inclusion as LMIC using text words and MeSH terms (appendix). Three investigators (TU-L, JJ, LM) were involved in reviewing all identified articles. Disagreements between reviewers were resolved by consensus.

We included articles reporting all-cause mortality following one of these interventions regardless of preoperative status, urgency of intervention, indication for procedure, or cause of death, and where the overall number of patients was recorded. Further information such as type of study, duration of the study, study size, and number of institutions involved was used to assess quality of the articles (see appendix for details on the methods used to assess quality and grade papers). We also searched available ministry reports for information about surgical mortality. We removed duplicate entries and screened identified articles to ensure they reported all necessary data. If needed data were used in the article but not directly reported, we contacted the authors for further information.

We excluded articles from countries other than those considered as LMICs in 2005. We also excluded studies that used the same sample population or study sample as larger or more recent studies, studies focused entirely on laparoscopic procedures, studies with insufficient data, or multicountry studies in which no

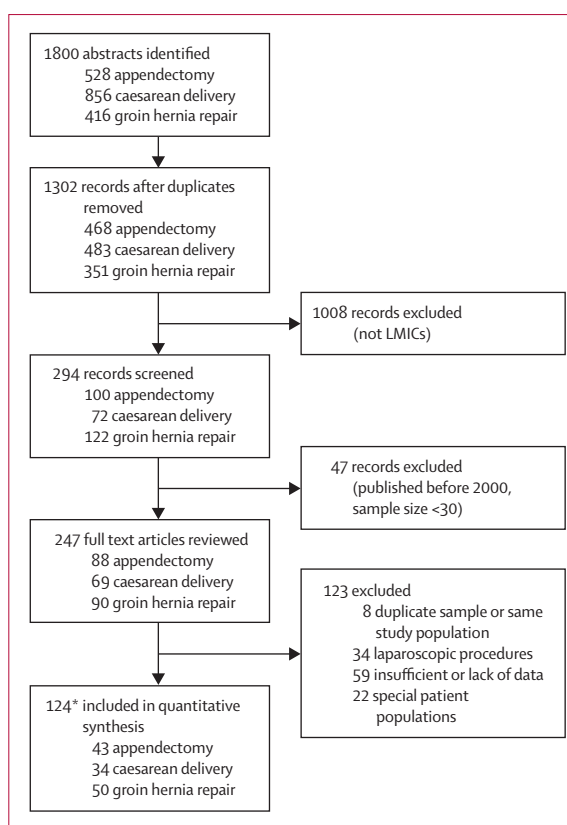


Figure 1: Study selection

LMICs=low-income and middle-income countries. *Total citations are not additive because one ministry report (Burkina Faso) provided mortality data for all three procedures and another ministry report (Bulgaria) did so for appendectomy and groin hernia repair.

See Online for appendix

	LMICs with surgical data (n=42)	LMICs without surgical data (n=71)	p value
LMICs in sample, by region			<0.0001
African	21 (50%)	19 (27%)	..
American	6 (14%)	10 (14%)	..
Eastern Mediterranean	7 (17%)	5 (7%)	..
European	2 (5%)	16 (23%)	..
Southeast Asian	5 (12%)	7 (10%)	..
Western Pacific	1 (2%)	14 (20%)	..
Median population size (millions)	21.1 (10.3–68.3)	5.8 (1.0–15.7)	0.04
Average life expectancy (years)	61 (1.5)	65 (1.0)	0.40
Population living in urban areas	43% (3.0)	45% (2.1)	0.40
Population younger than 15 years	37% (1.3)	33% (1.1)	0.36
Average number of physicians per 1000 population	0.58 (0.1)	1.37 (0.2)	0.78
Average number of nurses and midwives per 1000 population	1.2 (0.2)	2.9 (0.3)	0.32
Average GDP in 2008 (US\$)	2442 (543)	3254 (462)	0.45
Average per capita expenditure on health (US\$)	131 (25.2)	183 (21)	0.77
Estimated surgical rate per 100 000 population	1275 (208)	1830 (154)	0.92
Data are n (%), mean (SE), or median (IQR). p values from multivariate logistic regression model. LMICs=low-income and middle-income countries. GDP=gross domestic product.			
Table: Comparison of LMICs with and without reported surgical mortality data			

For more on RedCAP see <http://www.project-redcap.org>

specific country information could be obtained. We excluded studies with fewer than 30 patients based on an assumption of complication rates of 10% in these

settings in accordance with the rule of three sample size. Furthermore, sample sizes larger than 30 are commonly considered to be sufficient from a statistical standpoint.^{24,25} Finally, because our aim was to determine outcomes in a broadly generalisable population, we excluded studies of specific subsets of patients (eg, studies focusing only on HIV-positive patients). Data for number of patients, number of operations, number of deaths, number and type of other complications, and facility details were systematically extracted using RedCAP. For countries with surgical data from several studies, we aggregated the data to obtain larger sample sizes.

Model creation, validation, and statistical analysis

We used a two-step multiple imputation (MI) method to estimate mortality and CIs for countries with unknown data. We first established complete datasets for selected predictive variables using a fully conditional specification (FCS) MI method (appendix). This method has been described as an iterative algorithm that helps to address arbitrarily missing data and allows convergence on a prediction even when their exact distribution is unknown.²⁶ We used 100 imputations to achieve better nominal coverage for MI CIs in the substitution of missing data with imputed estimates.

After creation of these complete datasets, we used regression-based predictive mean matching (PMM) imputation to estimate mortality and confidence limits for countries without published mortality data. We included health expenditure, life expectancy, under-5 mortality, total population, physician density, surgical rate, and operating room density (by subregion) in all models. For caesarean delivery we also included maternal mortality, nurse and midwife density, and percentage of births by caesarean delivery; for appendectomy we included patients younger than 15 years. We validated the stability of the model by serially removing known mortality to assess whether estimates changed because of one value.

For every estimate, 95% CIs were derived from 100 MI results. Because of the heterogeneity of the available data, we aggregated results by GBD and WHO region to provide a more variable estimate of death, reflecting the heterogeneity of country-level information, service delivery, and health system organisation. We also compared surgical mortality estimates for each procedure against the Netherlands, a country with one of the lowest reported mortality for each of these procedures.^{27,28}

Data were analysed with SAS version 9.4.

Results

From an initial 1302 articles and reports identified, 247 full-text articles met our inclusion criteria, and 124 provided data for surgical mortality for at least one of the three selected operations (figure 1). We identified 34^{29–62} articles reporting caesarean mortality, representing

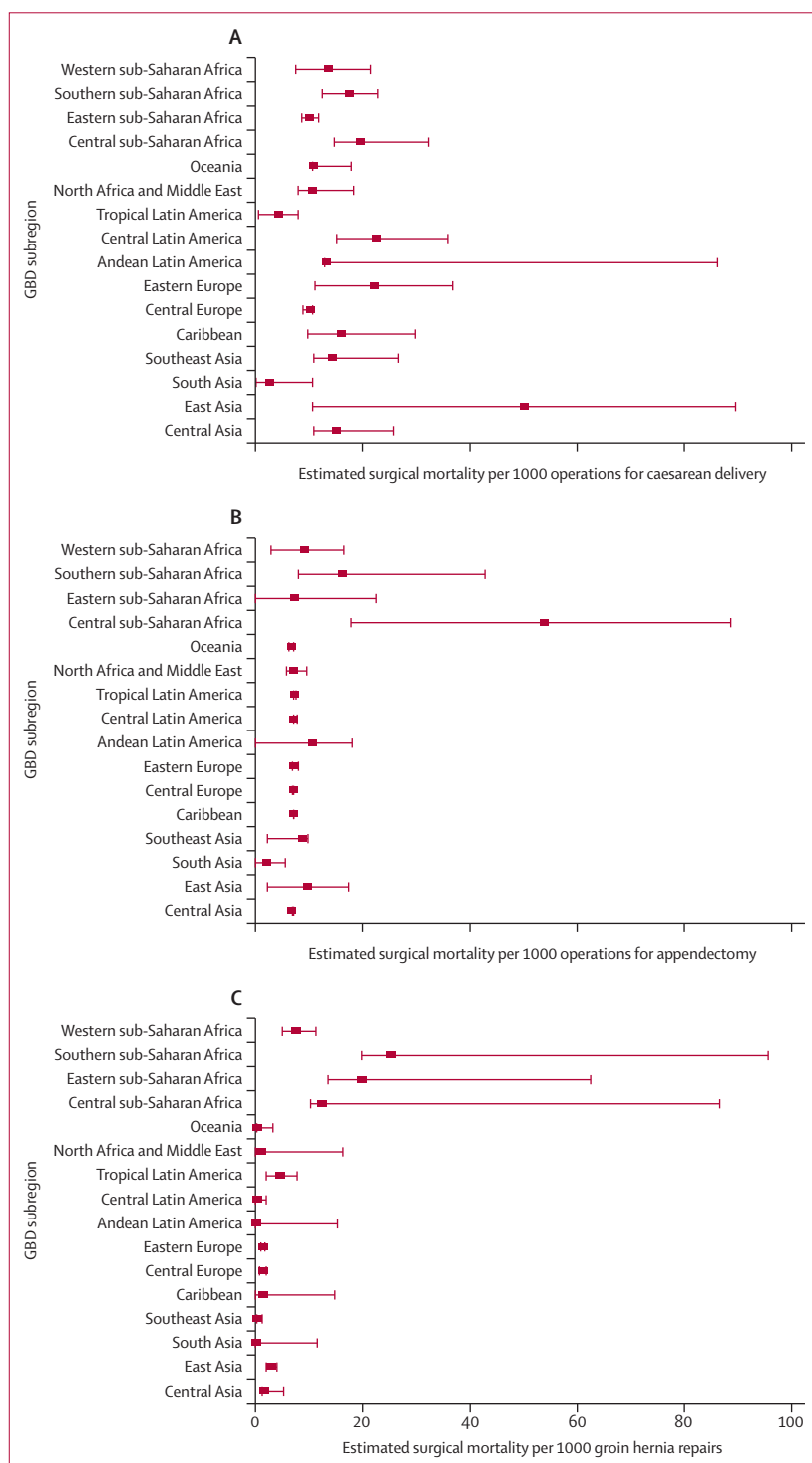


Figure 2: Estimated surgical mortality for caesarean delivery (A), appendectomy (B), and groin hernia repair (C) by Global Burden of Disease (GBD) subregion
Data are median (IQR).

23 countries, seven GBD regions, and four WHO regions; 43^{29,63–104} articles reporting appendectomy mortality, representing 20 countries, nine GBD regions, and six WHO regions; and 50^{29,92,105–152} articles reporting groin hernia repair mortality, representing 20 countries, eight GBD regions, and six WHO regions. 80 (65%) of 124 articles were considered high quality; articles of unacceptable quality were removed during our initial screening based on our exclusion criteria. Key characteristics of published articles and the results of the quality assessment can be found in the appendix (pp 7–13). From these articles we obtained surgical mortality data for 42 countries on at least one of the three selected operations. Reported surgical mortality ranged from 0 to 102.8 per 1000 caesarean deliveries (median 7.9 [IQR 2.8–19.9]), 0 to 88.6 per 1000 appendectomies (2.2 [0–17.2]), and 0 to 411.8 per 1000 groin hernias (4.9 [0–11.7]).

The characteristics of the countries with and without reported surgical mortality after adjustment for the covariates in the model are shown in the table. For each WHO region, the percentage of LMICs with and without reported data were significantly different ($p < 0.0001$), mainly driven by the absence of published data in the European and the Western Pacific regions (two and one countries with, and 16 and 14 countries without, respectively). Median population size (21.1 million vs 5.8 million for countries with and without data, respectively) was also significantly different between the two ($p = 0.04$). We noted no significant difference in the remaining economic or demographic characteristics for LMICs.

We estimated surgical mortality for all LMICs without reported data (appendix). After combining these estimates into GBD regions, median surgical mortality ranged from 2.8 (South Asia) to 50.2 (East Asia) per 1000 caesarean deliveries, 2.4 (South Asia) to 54.0 (Central sub-Saharan Africa) per 1000 appendectomies, and 0.3 (Andean Latin America) to 25.5 (Southern sub-Saharan Africa) per 1000 groin hernias (figure 2). Detailed summary statistics are shown in the appendix (pp 14–15).

The risk of death in many of these regions was significantly higher than in higher income settings. When compared with the Netherlands, which has a surgical mortality rate of 0.53 per 1000 caesarean deliveries,²⁸ 3.03 per 1000 appendectomies,²⁷ and 2.78 per 1000 groin herniorrhaphies,²⁷ the cumulative relative risk of death following surgical intervention based on WHO regional aggregation was 22.2, 2.4, and 1.87, respectively. Within each WHO region, median relative risk of death ranged from 20.4 (EMRO) to 27.0 (AMRO) per 1000 caesarean deliveries, 1.3 (SEARO) to 3.4 (AFRO) per 1000 appendectomies, and 0.1 (WPRO) to 5.0 (EMRO) per 1000 groin hernia repairs (figure 3). Detailed summary statistics are shown in the appendix (p 15).

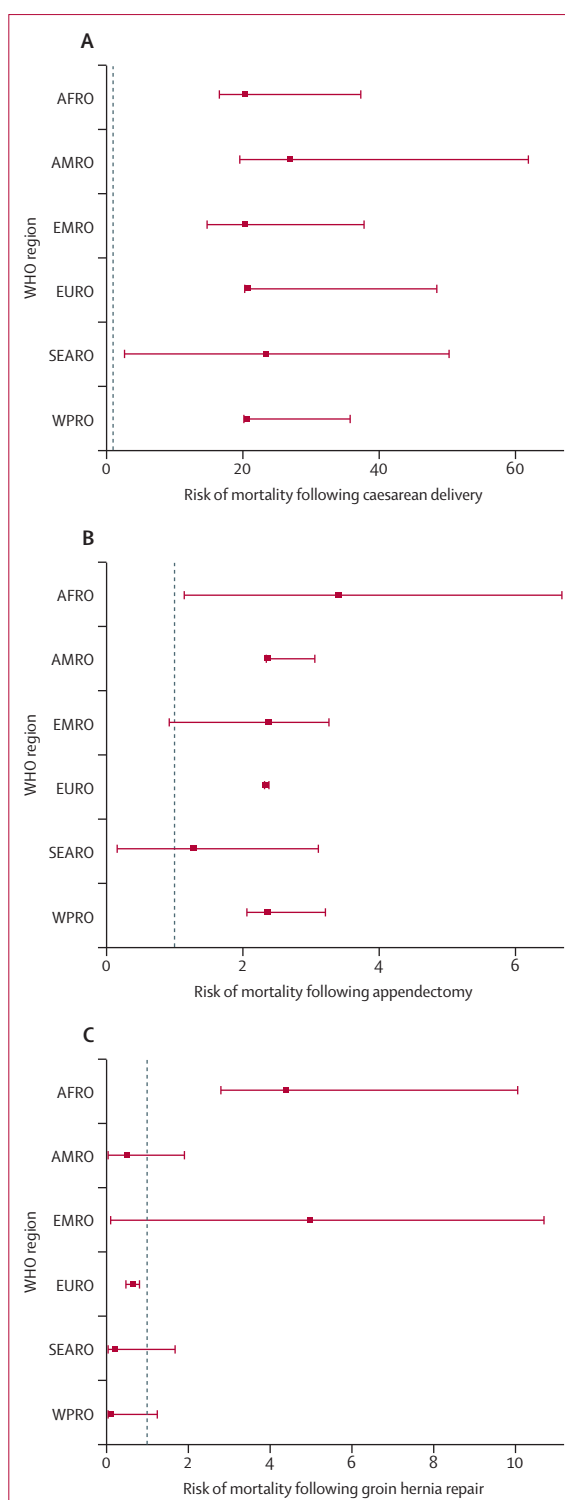


Figure 3: Relative risk of mortality following caesarean delivery (A), appendectomy (B), and groin hernia repair (C) by WHO region (compared with published surgical mortality from the Netherlands)
Point is median, error bars are IQR. AFRO=Regional Office for Africa. AMRO=Regional Office for the Americas. EMRO=Regional Office for the Eastern Mediterranean. EURO=Regional Office for Europe. SEARO=Regional Office for South-East Asia. WPRO=Regional Office for the Western Pacific.

Discussion

We noted that surgical mortality rates following caesarean delivery, appendectomy, and groin hernia repair are high and extremely variable across countries and settings, with rates as high as 103, 89, and 412 per 1000 operations, respectively. These results suggest a clear, pressing need to improve the outcomes of surgical care. Previous studies have shown substantial differences in postoperative mortality between countries, a finding we substantiate more broadly across developing settings.¹⁶

The cause of these widely divergent surgical mortality rates is probably multifactorial. In many LMICs, accessing a health facility with surgical capacity is challenging; delays are frequent and surgical conditions can be rapidly debilitating or fatal. Patients presenting later in their disease course have greatly altered physiology, including sepsis, dehydration, anaemia, and malnutrition. Operations undertaken under urgent circumstances are done so at much higher risk; anaesthetic administration is challenging, the stress of an operation is dangerous, and recovery is more likely to be complicated. The ability to support ailing patients in resource-poor settings is also a challenge, since complications following surgery must be recognised and effectively addressed.

However, there are several strategies to reduce deaths following surgery. Improving access to surgical care is a high priority. Delays due to both geography and financial expenditure can be reduced with appropriate policies aimed at improving triage and referral of sick surgical patients and reducing user fees.^{153–155} The effective implementation and use of surgical checklists has been shown to improve postoperative mortality, probably from improved communications and teamwork.¹⁵⁶ Improved anaesthetic preparation, administration, and monitoring are of utmost importance in providing safe perioperative care. Finally, in surgical practice, it is essential to monitor and evaluate outcomes, to fully assess causes of harm, and to generate strategies for improvement.

In view of this final point, this study's greatest limitation is a dearth of standardised data. With one exception, no LMIC reported overall mortality following surgical intervention. Thus we relied on individual studies and extrapolated to the broader population. Measuring and reporting outcomes of surgical intervention are difficult in the best of circumstances, but many LMIC health facilities are overburdened and incapable of longitudinal follow-up and tracking of results. We identified only 37% of LMICs with data for surgical mortality from even one centre, with many reporting no deaths in few studies of low sample size. The facilities and studies that reported such data were heterogeneous: they came from different geographic regions, environments, economies, and settings. They also reported on a heterogeneous group of patients, with differences in acuity of presentation and physiological compromise. However, facilities and surgical departments that were capable of tracking and reporting

such outcomes are probably more organised than many other facilities within their country. Additionally, death following surgery is often undocumented because patients might be lost to follow-up either within the hospital or following discharge, probably causing an underestimate of surgical mortality for these procedures. Mortality is typically reported only when it occurs as an inpatient during the same hospital admission as the operation; postoperative mortality based on length of stay was not systematically reported and could not be assessed.

Since our last literature search on Jan 15, 2015, we have identified 46 newly published studies: 19 on caesarean delivery, 20 on appendectomy, and seven on groin hernia repair. Only one article¹⁵⁷ met our inclusion criteria for caesarean delivery; the authors report surgical mortality from Médecins Sans Frontières facilities of 3.2 per 1000 caesarean deliveries in DR Congo, 3.1 per 1000 caesarean deliveries in Burundi, and 11.8 per 1000 caesarean deliveries in Sierra Leone. No data had been found for these countries in our analysis. There was one study of appendectomy¹⁵⁸ that met our inclusion criteria from Pakistan; this study reported no mortality. Finally, two studies on groin hernia repair met inclusion criteria: one¹⁵⁹ reported data for Cameroon and Mali, the other¹⁶⁰ reported data for Uganda; neither reported any surgical mortality. Our previous search had not identified data from Cameroon or Mali. The findings of these new articles are slightly lower than our estimates. We also identified six^{161–166} articles that aggregated caesarean mortality data from two or more countries; reported rates were quite variable, but we could not include them in this analysis as we could not link specific rates to individual countries.

Because of data limitations, we relied on a complex modelling strategy to estimate surgical mortality following these common procedures. Our model was hindered by low sample size and the use of national level data to provide country characteristics even though our data mostly came from individual facilities. However, even after adjustment for the type and size of facility, the results did not differ. There is also a concern of systematic reporting bias in the published literature; most probably, bias of this type would be towards non-reporting of poor outcomes, and as such would produce an underestimate of mortality. In view of our findings, we might in fact be under-reporting mortality. We did our literature search in English and also reviewed identified papers written in French and Spanish, but might have missed articles published in other languages that would have added more data to our study. Additionally, because our search went back as far as 2000, there might be recent systematic improvements that are not reflected by the earlier studies.

We had no way to evaluate the preoperative condition of patients who underwent surgery. Particularly with urgent surgery, patients at highest risk are also most likely to benefit from intervention. Comparing postoperative

mortality between facilities or countries as a means of showing safety lapses or inappropriateness of surgical intervention is improper because it does not adequately account for the premorbid condition of patients or the circumstances of their presentation. Our aim was not to show poor safety practices but rather to highlight the risks surgical patients face and the tremendously variable outcomes noted across different health systems. Importantly, there is also no way to quantify the number of patients who died from conditions typically treated by these surgical interventions but who never underwent an operation. Facilities that do not perform surgery have no cases, thus no postoperative fatalities. Yet many patients might benefit if such capacity were safely and effectively expanded.

Our findings quantify the variability in mortality following three of the most common operations—caesarean delivery, appendectomy, and groin hernia repair. Efforts to strengthen health systems in resource-poor settings will probably include improvements in surgical capacity and access, and corresponding improvements in surgical quality and safety will be essential to their development.

Contributors

TGW and AAG developed the idea for the study. TU-L, RF, ABH, and TGW designed the analysis plan. TU-L, JJ, LM, MME, and TGW acquired the data. TU-L, RF, MME, AAG, ABH, and TGW analysed and interpreted the data. TU-L and TGW drafted the report, which was critically reviewed by all authors.

Declaration of interests

We declare no competing interests.

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